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Tony N. Frudakis

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EXAMINER

MILLER, MARINA I

ART UNIT

PAPER NUMBER

1631

DATE MAILED: 11/20/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

10/644,594

Applicant(s)

FRUDAKIS ET AL.

Examiner

Marina Miller

Art Unit

1631

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 14 August 2006.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1,3-6,8,9,12,15,16,21,22,24,29-32,37,39-45 and 47-58 is/are pending in the application.
- 4a) Of the above claim(s) 12,15,16,21 and 22 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1,3-6,8,9,24,29-32,37,39-45 and 47-58 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
- ☐ Certified copies of the priority documents have been received.
 - ☐ Certified copies of the priority documents have been received in Application No. _____.
 - ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08)
Paper No(s)/Mail Date <u>8/14/06</u> . | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

Applicants' submission filed on 8/14/2006 is acknowledged.

Applicants elected with traverse SEQ ID NO:70 in the reply filed 11/21/2005. In light of the applicants' arguments regarding the art rejection under 35 U.S.C. 103(a), wherein applicants argue that prior art sequences are further required to be ancestry informative markers, the examiner extended her search from originally elected SEQ ID NO:70 to SEQ ID NOs:1, 3, 7, 8, 11, 21, 40, 59, 63, and 331. Upon review of the search, the examiner has determined that the prior art nucleotide sequences recited in the claims are not known to be ancestry informative markers. For this reason, the election of species requirement with regard to sequence election (*i.e.*, election of one SEQ ID NO) is hereby withdrawn and claims 6 and 37 are rejoined.

Claims 1, 3-6, 8-9, 12, 15-16, 21-22, 24, 29-32, 37, 39-45, and 47-58 are pending.

Claims 2, 7, 10-11, 13-14, 17-20, 23, 25-28, 33-36, 38, 46, and 59-82 are cancelled.

Claims 12, 15-16, and 21-22 are withdrawn again from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected Invention and species, there being no allowable generic or linking claim. Election was made with traverse in the response filed 11/21/2005.

Claims 1, 3-6, 8-9, 24, 29-32, 37, 39-45, and 47-58 presently are under examination.

Applicants' arguments have been fully considered. Rejections and/or objections not reiterated from previous office actions are hereby withdrawn. The following rejections and/or objections are applied.

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Claim Objections

Claims 12, 15-16, and 21-22 are objected to because of the following informalities: the claims were withdrawn in the office action mailed 9/22/2005; however, the claims are identified as "original". Applicants are advised to carefully review the status of the claims in future amendments.

Information Disclosure Statement

The Information Disclosure Statement (IDS) filed 8/14/2006 has been considered in full.

Claim Rejections - 35 USC § 101

35 U.S.C. 101 reads as follows:

Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

Claims 1, 3-6, 8-9, 24, 29-32, 37, 39-45, and 47-58 are rejected under 35 U.S.C. 101 because the claimed invention is directed to non-statutory subject matter.

Claim 1 recites a method for inferring a trait of an individual comprising detecting, in a nucleic acid sample from an individual, nucleotide occurrences of SNPs in a panel of AIMs and identifying the population structure, wherein identifying infers the trait. However, not all processes are statutory under 35 U.S.C. 101. See MPEP 2106 (Section IV in particular). To satisfy 101 requirements, the claim must be for a practical application, which can be met if the claimed invention "transforms" an article or physical object to a different state or thing OR the claimed invention otherwise produces a useful, concrete, and tangible result. If claims are directed to abstract ideas (such as mathematical algorithms), natural phenomena, and laws of nature, the claims must be considered as a whole for determining whether an abstract ideas, natural phenomena, or laws of nature has a particular application.

In the instant case, the claimed method does not transform or reduce an article or a physical object (*e.g.*, a molecule, a sample, a signal produced by labels, *etc.*) to a different stage or thing. Specifically, the step of “detecting, in a nucleic acid sample from an individual, nucleotide occurrences of SNPs in a panel of AIMs” does not necessarily comprise contacting a sample with oligos, hybridizing a sample comprising nucleic acids with oligos, or purifying nucleic acids (a sample of nucleic acid) from a sample. One may have hybridized a sample and oligos and derived hybridization data at earlier time wherein the resultant data was stored on a computer. At a later time, nucleotide occurrences of SNPs may be determined by comparing the stored data with, for example, a database of SNPs. Thus, “determining” SNPs by the instant method may be entirely within a computer, and therefore the method does not transform or reduce an article or a physical object to a different stage or thing. The claims do not recite tangible expression (*i.e.*, real-world result) of identifying a population structure or inferring a trait in a form useful to one skilled in the art. Thus, the method does not recite either a physical transformation of matter or a step of producing something that is concrete, useful, and tangible, and is not statutory.

Claim Rejections - 35 USC § 112

First Paragraph

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1, 3-6, 8-9, 24, 29-32, 37, 39-45, and 47-58 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains

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subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This is a NEW MATTER rejection.

Claims 1, 24, 31, 39-42, 45, 50, 53, and 56, as amended, recite that SNPs detected in a sample from an individual are indicative of a population structure. However, a population structure indicated by SNPs detected in a test sample does not have support in the specification, claims, or drawings, as originally filed. Applicants do not point to support in the originally filed disclosure for the claim amendments, and none is apparent. The specification only discloses, for example on pages 10, 24, and 40, that AIMs are genetic loci that show alleles with high frequency differences between populations. The original claims also recite that AIMs are indicative of population structure. The original specification and claims do not disclose that SNPs detected in a sample from an individual are indicative of a population structure. For these reasons, the claims are rejected for reciting new matter.

Enablement

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

There are many factors to be considered when determining whether there is sufficient evidence to support a determination that a disclosure does not satisfy the enablement requirement and whether any necessary experimentations is "undue." These factors include, but are not limited to:

- a) The breadth of the claims;
- b) The nature of the invention;

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- c) The state of the prior art;
- d) The level of one of ordinary skill;
- e) The level of predictability in the art;
- f) The amount of direction provided by the inventor;
- g) The existing of working examples; and
- h) The quantity of experimentation needed to make or use the invention based on the content of the disclosure.

In re Wands, 858 F.2d 731, 737 (Fed. Cir. 1988).

The Board also stated that although the level of skill in molecular biology is high, the results of experiments in genetic engineering are unpredictable. 858 F.2d at 740. While all of these factors are considered, sufficient amount for a prima facie case are discussed below.

Claim1, 3-6, 8-9, 24, 29-32, 37, 39-45, and 47-58 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for specific AIM panels disclosed in the specification (*e.g.*, in tables 1-3 and 6) and recited in the instant claims (claims 4-6 and 37), does not reasonably provide enablement for an AIM panel of unknown specificity. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims..

a) The claims are broad because they are drawn to methods for inferring a trait of an individual and estimating proportional ancestry of an individual (*see* claims 1 and 31) comprising detecting SNPs in a sample from an individual, wherein the SNPs are indicative of a population structure, and wherein the population structure is correlated with a trait of the individual. The instant specification does not provide specific guidance to practice the invention because it does not disclose how to infer a trait of an individual without knowing how to select or set up an AIM panel or of what population structure a panel indicates. The instant specification provides guidance to how to practice the invention only for specific AIM panels discloses in the

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specification. Also, the instant specification does not disclose how to infer a trait of an individual wherein SNPs from a test sample of an individual, not AIM panels, are indicative of a population structure.

b) The invention is drawn to a method for inferring a trait and estimating proportional ancestry of an individual.

c, e) A prior art analysis shows that a panel of known markers indicative of ethnic affiliation (population-specific markers) are used for inferring a trait of an individual in an admixed population. See Shriver, *Am. J. Hum. Genet.*, 60:957-964 (1997); Parra, *Am. J. Hum. Genet.*, 63:1839-51 (1998); McKeigue, *Ann. Hum. Genet.*, 64:171-186 (2000). The prior art also shows that ancestral markers may define a population structure (*e.g.*, Africans, Europeans, Amerindians, European Americans, African Americans, Hispanic Americans, *etc.*) and teaches that a nucleotide in a SNP position of a marker can be detected and compared to the nucleotide in the marker, to thereby determine an ethnic affiliation of an individual. Parra, *Am. J. Hum. Genet.*, 63:1839-51 (1998). The prior art does not teach how to infer a trait of an individual for an unknown AIM panel. The prior art also does not teach that SNPs from a test sample of an individual, not AIM panels, are indicative of a population structure.

d) The skill of those in the art of molecular biology and bioinformatics is high.

f) The specification does not provide guidance for inferring a trait of an individual without knowing what population structure a panel of markers indicates.

g) The specification provides working examples wherein a known panel of ancestral markers, which are specific for, for example, American, African, European, and Hispanic

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populations, is used for inferring a trait of an individual (*e.g.*, examples 1-2). The specification does not provide working examples wherein an AIM panel is unknown.

h) In order to practice the claimed invention, one skilled in the art must randomly select a panel of markers and must guess which parameters to use for inferring a trait of an individual.

This constitutes undue experimentation.

Due to the undue experimentation required to obtain the goal of the invention, the lack of directions presented in the specification, the complex nature of the invention, and the state of the prior art showing a use of known markers indicative of a population structure, the specification fails to teach one skilled in the art how to use the claimed method for inferring a trait and estimating proportional ancestry of an individual wherein the AIM panel is unknown.

Second Paragraph

Claims 1, 3-6, 8-9, 24, 29-32, 37, 39-45, and 47-58 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 1, as amended, recites “a trait” in line 9. Claim 1 also recites “a trait” in line 2. It is not clear whether “a trait” recited in lines 2 and 9 are the same or different. Claim 1 also recites “the trait” in lines 17 and 18. It is not clear which trait is intended, “a trait” recited in line 2 or in line 9 (if different). As the intended limitations are not clear, claims 1, 3-6, 8, 24, and 29-30 are indefinite.

Claims 3 and 24 recite “the trait”. Claims 3 and 24 depend from claim 1. It is not clear what trait is intended, “ “a trait” recited in claim 1 in line 2 or in line 9 (if different). As the intended limitation is not clear, claims 3-6, 8-9, 24, and 29-30 are indefinite.

Claim 1, as amended, recites in the preamble “a method of inferring.” The claim further recites steps of detecting SNPs and identifying population the structure, “wherein identifying the population structure infers the trait, thereby inferring the trait.” It is not clear whether the limitations “wherein identifying the population structure infers the trait” and/or “thereby inferring the trait ” are intended to be an active, positive step(s) of the method, or merely an intended use of the identified population structure. Further, because it is not clear whether the method comprises an active positive step of “inferring the trait,” the relation between the preamble and the method steps is still not clear.

Applicants argue that the limitation of claim 1, as amended, “wherein identifying the population structure infers the trait” recites an active step, *i.e.*, “infers”.

In response it is noted that it is not clear whether “identifying” IS “inferring” OR “inferring” requires some additional steps, algorithms, or models in order to “infer” a trait from the identified population structure, *e.g.*, the result of identifying is used in an algorithm by which a trait is “inferred”. Moreover, if step (b) has already “inferred” a trait, as asserted by applicants, then it is not clear what limitation is intended by reciting the phrase “thereby inferring the trait” subsequently to step (b).

As the intended limitation is not clear, claims 1, 3-6, 8, 24, and 29-30 are indefinite.

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Claim 1, as amended, recites in step (a) detecting SNPs in a panel of AIMS, wherein SNPs are indicative of a population structure. Claim 1 further recites in step (b) identifying the repopulation structure indicated by SNPS detected in step (a). It is not clear what limitation is intended by reciting step (b) because the step is redundant, *i.e.*, SNPs indicative of the population structure has been identified in step (a). As the intended limitation is not clear, claims 1, 3-6, 8, 24, and 29-30 are indefinite.

Claims 1 and 31, as amended, recite the limitation “one AIM that is not linked to a gene linked to the trait.” It is not clear what limitation is intended because the claims earlier recite that a population structure is indicated by AIMS and is correlated with a trait (*i.e.*, AIMS are linked to a trait). As the intended limitation is not clear, claims 1, 3-6, 8-9, 24, 29-32, 37, 39-45, and 47-58 are indefinite.

Claims 4-6 recite the limitation “wherein the panel comprises AIMS set forth as” SEQ ID NOs:1 to 331, 1 to 71, and three panels of various SEQ ID NOs. It is not clear whether a panel comprises all the recited SEQ ID NOs or a subset thereof. If the latter, then is not clear which sequences are intended to be comprised within the subset. As the intended limitation is not clear, claims 4-6 are indefinite.

Claim 24, as amended, recites the limitation “wherein the sub-population structure infers *with* the trait.” It is not clear what limitation is intended, *e.g.*, the structure corresponds to the trait, structure is used in an algorithm by which the trait is inferred, *etc.* It is further unclear whether the limitation “wherein the sub-population structure infers with the trait” is intended to be an active, positive step(s) of the method, or merely an intended use of the identified sub-

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population structure. It is further unclear what steps, algorithms, or models are used for “inferring.” As the intended limitation is not clear, claim 24 is indefinite.

Claim 31, as amended, recites in the preamble “a method of estimating.” The claim further recites steps of detecting SNPs and identifying population the structure, “wherein identifying the population structure estimates proportional ancestry, thereby estimating proportional ancestry.” It is not clear whether the limitations “wherein identifying the population structure estimates proportional ancestry” and/or “thereby estimating proportional ancestry” are intended to be an active, positive step(s) of the method, or merely an intended use of the identified population structure. Further, because it is not clear whether the method comprises an active positive step of “estimating proportional ancestry,” the relation between the preamble and the method steps is still not clear.

Applicants argue that the limitation of claim 31, as amended, “wherein identifying the population structure estimates proportional ancestry” recites an active step, *i.e.*, “estimates”.

In response it is noted that it is not clear whether “identifying” IS “estimating” OR “estimating” requires some additional steps, algorithms, or models in order to “estimate” proportional ancestry, *e.g.*, the result of identifying is used in an algorithm by which proportional ancestry is “estimated”. Moreover, if step (b) has already “estimated” proportional ancestry, as asserted by applicants, then it is not clear what limitation is intended by reciting the phrase “thereby estimating proportional ancestry” subsequently to step (b).

As the intended limitation is not clear, claims 31-32, 37, 39-45, and 47-58 are indefinite.

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Claim 31, as amended, recites in step (a) detecting SNPs in a panel of AIMs, wherein SNPs are indicative of a population structure. Claim 31 further recites in step (b) identifying the population structure indicated by SNPs detected in step (a). It is not clear what limitation is intended by reciting step (b) because the step is redundant, *i.e.*, SNPs indicative of a population structure have already been identified in step (a). As the intended limitation is not clear, claims 31-32, 37, 39-45, and 47-58 are indefinite.

Claim 45, as amended, recites the limitation “wherein the sub-population structure infers ethnicity of the test individual.” It is unclear whether the limitation “wherein the sub-population structure infers” is intended to be an active, positive step(s) of the method, or merely an intended use of the identified sub-population structure. It is further unclear what steps, algorithms, or models are used for “inferring.” Further, claim 45 depends from claim 31 which is directed to a method of estimating proportional ancestry comprising steps of detecting SNPs and identifying the population structure wherein the structure estimates proportional ancestry. It is not clear where “inferring ethnicity” recited in claim 45 fits within the steps of claim 31. As the intended limitation is not clear, claims 45 and 47 are indefinite.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

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Claims 1, 3, 8, and 31-32 are rejected under 35 U.S.C. 103(a) as being unpatentable over McKeigue, *Ann. Hum. Genet.*, 64:171-186 (2000), in view Hanis, *Am. J. Physical Anthropol.*, 70:433-441 (1986).

McKeigue discloses estimating admixture in African-American population. (abstract) McKeigue discloses ten ancestry markers (p. 174). McKeigue discloses contacting a sample with oligonucleotides that can detect polymorphism because McKeigue discloses detecting polymorphism by using PCR which necessarily comprises oligonucleotides (p. 174, left col.). McKeigue discloses genotyping SNP markers (p. 182). McKeigue discloses identifying a population structure that correlates with ancestry markers and with a trait (p. 174, left col. and p. 177-178) thereby inferring the trait of the individual (p. 178). McKeigue discloses identifying with a predetermined level of confidence (tables 1-2 and p. 173). Thus, McKeigue discloses steps similar to those of instant claim 1. McKeigue also discloses biogeographical ancestry (BGA) trait (p. 175), similar to that of instant claims 3 and 31.

McKeigue does not disclose AIMs not linked to genes linked to a trait.

Hanis discloses estimating individual admixture based on ancestral markers wherein a marker does not detect a disease (a trait, *i.e.*, diabetes and gallbladder), but detects ancestry (ancestral marker) (p. 437-439). Hanis conducts his research for Native American, African, Mexican-American, and European ancestral groups.

It would have been obvious to one of ordinary skill in the art at the time of the instant invention to modify the method of McKeigue to use AIM that are not linked to a gene linked to a trait for a population having Native American, African, Mexican-American, and European ancestry, such as taught by Hanis, where the motivation would have been to estimate the

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relationship of individual admixture to diabetes and gallbladder disease status, as taught by Hanis, p. 433 and 437.

Answer to arguments

Applicants argue that McKeigue does not disclose SNPs located outside of genes.

In response, it is noted that the rejection is made under 35 U.S.C. 103(a) over the combination of references, wherein Hanis does disclose AIMs not linked to a gene linked to a trait, as set forth above. It is also noted that the instant claims do not recite SNPs located outside of genes. Motivation to combine the references is set forth above.

Claims 1, 3, 8, 31-32, and 39 are rejected under 35 U.S.C. 103(a) as being unpatentable over Parra, *Am. J. Physical Antropol.*, 114-118 (2001), in view Hanis, *Am. J. Physical Anthropol.*, 70:433-441 (1986).

Parra discloses a method for inferring ancestral proportions and admixture in African-Americans (abstract). Parra discloses ten ancestry markers (p. 20 and table 1). Parra discloses contacting a sample with oligonucleotides that can identify SNPs (PCR, p. 20, left col.). Parra discloses identifying a population structure that correlates with ancestry markers and with a trait (table 1, fig. 1, p. 22). Parra discloses identifying with a predetermined confidence interval (p. 21). Thus, Parra discloses steps similar to those of instant claim 1. Parra discloses BGA trait (fig. 1 and p. 25), similar to that of instant claims 3 and 31. Parra discloses calculating individual admixture proportions using a maximum likelihood method of Chakraborty (p. 20 and 21-22), similar to that of instant claim 39.

Parra does not disclose AIMs not linked to genes linked to a trait.

Hanis discloses estimating individual admixture based on ancestral markers wherein a marker does not detect a disease (a trait, *i.e.*, diabetes and gallbladder), but detects ancestry (ancestral marker) (p. 437-439). Hanis conducts his research for Native American, African, Mexican-American, and European ancestral groups.

It would have been obvious to one of ordinary skill in the art at the time of the instant invention to modify the method of Parra to use AIM that are not linked to a gene linked to a trait for a population having Native American, African, Mexican-American, and European ancestry, such as taught by Hanis, where the motivation would have been to estimate the relationship of individual admixture to diabetes and gallbladder disease status, as taught by Hanis, p. 433 and 437.

Answer to arguments

Applicants argue that Parra does not disclose phenotypes or physical traits, but discloses identification of the parental population (African or European). Applicants further argue that the instant method is based on the association between population and an actual phenotype (trait). Applicants also argue that Parra only recites SNPs located within genes linked to a trait, rather than outside of coding sequences linked to a trait.

In response to the argument, it is noted that the instant claims do not recite "phenotype or physical trait," but only recite "a trait." It is further noted that the instant claims do not recite SNPs located outside of coding sequences of genes linked to a trait. Also, the rejection is made under 35 U.S.C. 103(a) over the combination of references, wherein Hanis does disclose AIMs not linked to a gene linked to a trait, as set forth above. Motivation to combine the references is set forth above.

Claims 1, 3, 8, 24, 30-32, 45, and 50-52 are rejected under 35 U.S.C. 103(a) as being unpatentable over Sorenson, US 2003/0172065, in view of in view Hanis, *Am. J. Physical Anthropol.*, 70:433-441 (1986).

Sorenson discloses a method of determining ancestral proportions and admixture in the diverse population (fig. 4). Sorenson discloses contacting a sample with oligonucleotides (PCR; fig. 4 and [0039]) wherein oligos can detect SNPs ([0042] and table 1 showing a panel of at least ten ancestry markers and oligonucleotides for the identification of SNPs). Sorenson discloses identifying a population structure (fig. 4 and [0032], [0046]-[0047]) that correlates with markers and a trait. Sorenson discloses identifying a population structure with a predetermined confidence interval and statistical probability [[0048], [0061]. Thus, Sorenson discloses steps similar to those of instant claim 1. Sorenson also discloses a trait of BGA [0012], [0032], similar to that of claims 3 and 31. Sorenson discloses identifying a subpopulation structure (members of one group) [0047], similar to that of instant claims 24 and 45. Sorenson teaches that thousands of known genetic markers and millions of characterized SNPs may be analyzed [0042], similar to that of instant claim 30. Sorenson discloses comparing of the nucleotide occurrence of markers with known proportional ancestry, and specifically the occurrence that is contained in a database ([0017], [0020], [0047] and fig. 4, claims 1, 6-7, 9, 13-18), similar to that of instant claims 50-52. Sorenson discloses a large list of human ancestral markers (tables 1-4).

Sorenson does not disclose AIMs not linked to genes linked to a trait.

Hanis discloses estimating individual admixture based on ancestral markers wherein a marker does not detect a disease (a trait, *i.e.*, diabetes and gallbladder), but detects ancestry

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(ancestral marker) (p. 437-439). Hanis conducts his research for Native American, African, Mexican-American, and European ancestral groups.

It would have been obvious to one of ordinary skill in the art at the time of the instant invention to modify the method of Sorenson to use AIM that are not linked to a gene linked to a trait for a population having Native American, African, Mexican-American, and European ancestry, such as taught by Hanis, where the motivation would have been to estimate the relationship of individual admixture to diabetes and gallbladder disease status, as taught by Hanis, p. 433 and 437.

Answer to arguments

Applicants argue that Sorenson is not a proper prior art reference because it was published on 9/11/2003, after the filing date of the instant application, which is 8/19/2003.

In response, it is noted that Sorenson is a US application published 9/11/2003 but filed 3/29/2002 which also claims priority to a provisional application filed 3/30/2001. The earliest priority claimed by applicants is 5/28/2002. Thus, Sorenson properly qualifies as prior art as its filing date is earlier than the filing date of the instant application.

Claim 9 is rejected under 35 U.S.C. 103(a) as being unpatentable over Sorenson, US 2003/0172065, in view Hanis, *Am. J. Physical Anthropol.*, 70:433-441 (1986), as applied to claims 1, 3, 8-9, 24, 30-32, 45, and 50-52 above, in view of Collins-Schramm, *Am. J. Hum. Genet.*, 70:737-750 (2/11/2002), and further in view of Kanetsky, *Am. J. Hum. Genet.*, 70:770-775 (2/6/2002).

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Sorenson and Hanis make obvious the method of claims 1, 3, 8-9, 24, 30-32, 45, and 50-52, as set forth above.

Sorenson and Hanis do not specifically disclose the BGA comprising a proportion of three ancestral groups selected from sub-Saharan African, Native America, Indo-European, or East Asian ancestral groups.

Collins-Schramm discloses ancestral markers for mapping by admixture linkage disequilibrium for the population comprising African (Zimbabwe, *i.e.*, sub-Saharan Africa), Amerindian, European, and Mexican ancestry (abstract).

Sorenson, Hanis, and Collins-Schramm do not specifically teach BGA from Asian ancestral groups.

Kanetsky discloses white, African, Spanish, Hispanic, Native Indian, Aboriginal, and Asian ancestry (p. 772).

It would have been obvious to one of ordinary skill in the art at the time of the instant invention to modify the method of Sorenson and Hanis to use BGA comprising at least three groups from various ancestral groups, such as taught by Collins-Schramm and Kanetsky, where the motivation would have been to determine ancestral proportions of different groups of Americans for mapping complex genetic diseases, as taught by Collins-Schramm, p. 737.

Claims 29 is rejected under 35 U.S.C. 103(a) as being unpatentable over Sorenson, US 2003/0172065, in view of Hanis, *Am. J. Physical Anthropol.*, 70:433-441 (1986), as applied to claims 1, 3, 8-9, 24, 30-32, 45, and 50-52 above, in view of Akey, *BioTechnique*, 30(2):358-367 (2001).

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Sorenson and Hanis make obvious the method of claims 1, 3, 8-9, 24, 30-32, 45, and 50-52, as set forth above.

Although Sorenson teaches that thousands of known genetic markers and millions of characterized SNPs may be analyzed, Sorenson and Hanis do not specifically teach high-throughput methods.

Akey discloses a high-throughput genotyping technique (abstract).

It would have been obvious to one of ordinary skill in the art at the time of the instant invention to modify the method of Sorenson and Hanis to use high-throughput methods, such as taught by Akey, where the motivation would have been to improve genetic mapping, as taught by Akey, p. 358.

Claims 40-43 are rejected under 35 U.S.C. 103(a) as being unpatentable over of Parra, *Am. J. Physical Antropol.*, 114-118 (2001), in view Hanis, *Am. J. Physical Anthropol.*, 70:433-441 (1986), as applied to claims 1, 3, 8-9, 31-32, and 39 above, in view of Pritchard, *Theoretical Population Biology*, 60:227-237 (2001).

Parra and Hanis make obvious the method of claims 1, 3, 8-9, 31-32, and 39, as set forth above.

Parra and Hanis do not disclose a multiple way comparison and a graphical representation.

Pritchard discloses statistical methods for determining the population structure and admixture. Pritchard discloses generating graphical representation of the comparison of three ancestral groups wherein ancestral groups are represented by a vertex of a triangle, and wherein

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the maximum likelihood of proportional affiliation for an individual comprises a point within the triangle (fig. 1 and p. 232-233). Pritchard discloses six two-way analysis (1-2; 2-1; 2-3; 3-2; 1-3; and 3-1) (fig. 1). Pritchard discloses three three-way analyses (1-2-3; 2-3-1; and 3-2-1).

It would have been obvious to one of ordinary skill in the art at the time of the instant invention to modify the method of Parra and Hanis to conduct multiple way analysis of the likelihood of ethnic affiliations and graphically represent the result, such as taught by Pritchard, where the motivation would have been to avoid an influence of a high rate association of markers and time consuming and expensive assembling of family-based samples, as taught by Pritchard, *see* Introduction, p. 227-228.

Claim 48 is rejected under 35 U.S.C. 103(a) as being unpatentable over Sorenson, US 2003/0172065, in view of Hanis, *Am. J. Physical Anthropol.*, 70:433-441 (1986), as applied to claims 1, 3, 8-9, 24, 30-32, 45, and 50-52 above, in view of Pritchard, *Genetics*, 155:945-959 (2000).

Sorenson and Hanis make obvious the method of claims 1, 3, 8-9, 24, 30-32, 45, and 50-52, as set forth above.

Sorenson and Hanis do not specifically disclose generating an ancestral map.

Pritchard discloses statistical methods for determining the population structure and admixture (abstract). Pritchard discloses an ancestral map and the correspondence to the proportional ancestry (fig. 3 and fig. 6).

It would have been obvious to one of ordinary skill in the art at the time of the instant invention to modify the method of Sorenson and Hanis to generate an ancestral map, such as

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taught by Pritchard, where the motivation would have been to test for clustering for samples representing distinct populations, as taught by Pritchard, p. 951.

Evidence of Non-Obviousness submitted by applicants.

Applicants submitted publications in peer-reviewed journals (exhibits A-D) as additional indicia of non-obviousness.

In response to arguments that the exhibits indicate commercial success, it is noted that the claims are merely directed to a method of inferring a trait of an individual, which is not limited to be used in a forensic or criminal justice application. As such, evidence of success in a criminal justice application is not a point of patentability for the instant claims. Evidence indicating that one or more persons had “never heard of” using ancestry evaluation in a criminal justice application is neither evidence of a “long-felt need” nor is it evidence of “failure of others” to successfully perform the CLAIMED method steps. In fact, the prior art indicates that “others” have indeed successfully used AIMS in methods to determine or “infer” proportions of ancestral traits, as set forth above. In view of the teaching of the prior art, the arguments that the claimed method provides an “unexpected result” are not persuasive. The examiner cannot find any evidence of “teaching away” from the claimed invention in the exhibits filed, contrary to applicant’s arguments.

Conclusion

No claims are allowed.

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Any inquiry concerning this communication or earlier communications from the examiner should be directed to Marina Miller whose telephone number is (571)272-6101. The examiner can normally be reached on 8-6, M-Thu.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Andrew Wang, Ph. D. can be reached on (571)272-0811. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

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Art Unit 1631

MM